

invention is different than that of co-pending application '035 and thus, the two applications are considered distinct.

Claim 7 has been rejected under 35 U.S.C. §112, second paragraph. The claim has been amended to obviate this rejection.

Claims 1-19 have been rejected under 35 U.S.C §103(a) as being unpatentable over Elango et al., U.S. Patent No. 4,981,995 in view of Chaudhari et al., U.S. Patent No. 6,093,847.

The Examiner's rejection is respectfully traversed.

The claims as amended are directed to a process for the preparation of 2-aryl propionic acids comprising the steps of reacting an aryl compound with an organic acid, water and a palladium catalyst in an organic solvent in a carbon monoxide atmosphere under homogeneous conditions. The reaction mixture is cooled to an ambient temperature wherein the reaction vessel is flushed with an inert gas. The solvent is removed by conventional methods, the catalyst is separated and the 2-aryl propionic acid is isolated.

Elango et al. '995 is directed to a method of preparing ibuprofen. The Examiner has pointed out that the differences in the instant invention versus Elango et al. '995 is that in the present invention tetrabutyl ammonium halide is being used as a halide promoter; that the range of water used is 1 to 6% (v/v) of the total mixture; and flushing with an inert gas after the reaction is completed. It is important to note that another difference between the present invention and Elango et al. '995 is that the pressure used in the process step of Elango et al. is at least 500 psig whereas in the present invention it can be as low as 50 psig, to achieve the same end result. Thus, the present invention has the advantage of providing mild conditions for the operation of the process.

Additionally, the ligands of the catalyst used in Elango et al.'s process are different than the ligands of the catalyst of the present invention. The chemical nature of the ligand incorporated in the catalyst plays an important role in determining the rate of reaction, reactivity of the catalyst, reaction condition to be used and specificity of the obtained product. Hence, each catalyst used would have an optimum condition for operation with respect to the above-mentioned factors. Such optimum conditions can only be achieved by performing many reactions involving logical permutation combinations of these factors to achieve the desired results. Hence, it has taken a long time and a lot of human effort to achieve the objective of the present invention. The outcome of the present invention is not the result of any obvious suggestion arising from prior art knowledge.

The Examiner has stated that in the present invention, the reaction vessel is flushed with an inert gas after the reaction process, whereas Elango et al.'s reference teaches the flushing step before initiation of the reaction process. The Examiner concludes that this is merely reversing the order of steps in a multiple step process and thus is not a patentable modification because of the absence of unexpected or non-obvious results. The Applicants disagree with the Examiner's statement in that they do not feel that this is mere reversibility of the steps of the process because there are many possible differences that would arise in respect to the profile of the end product when the reaction is performed in an inert atmosphere and in absence of an inert atmosphere maintaining all of the parameters of the process conditions deemed identical. An inert atmosphere provides a condition wherein susceptibility to oxidation of the substrate and other reactants used is minimized, resulting in a cleaner end-product with high purity and yield. Alternatively, the other possibilities being, in the absence of an inert atmosphere the end product formed could also be susceptible to deterioration to produce low

purity and yield of the required product. In the present invention, if inert atmosphere is not maintained after the formation of this desired product, the 2-aryl propionic acid obtained may tend to undergo decarboxylation, which yields undesired products. Hence, it is more appropriate to use the flushing of an inert gas after the completion of the reaction to achieve better output of the desired objective.

Whereas, Chaudhari '847 is directed to the preparation of ibuprofen from 2-arylalcohol using a catalyst comprising group VIII metal and semilabile anionic chelating ligand containing a "N" donor and an O. The semilabile anionic chelating ligand imparts efficacy to the performance of the catalyst used in the process. However, the catalyst used in the present invention is different and does not contain ligand of semilabile nature to enhance the efficacy of the catalyst performance in the process adopted. Thus, one skilled in the art cannot envision any obvious suggestion to use the bidentate palladium catalyst in the present invention to generate 2-aryl propionic acid from 2-arylalkylhalide and also being associated with an equivalent efficacy of the prior art.

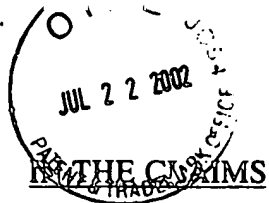
In view of the foregoing, the Applicants contend that the amended claims and the claims dependent therefrom are in proper form. Applicants also respectfully contend that the teachings of Elango et al. '995 in view of Chaudhari et al. '847 do not establish a *prima facie* case of obviousness under 35 U.S.C. § 103(a). Thus, claims 1-19 are considered to be patently distinguishable over the prior art of record.

The application is now considered to be in condition for allowance, and an early indication of same is earnestly solicited.

Respectfully submitted,

A handwritten signature in cursive script, appearing to read "Arlene J. Powers", is written over a horizontal line.

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Claim 1 has been amended as follows:

1. An improved process for the preparation of 2-aryl propionic acids, ~~[which comprises~~
~~the]~~ the said process comprising steps of:
- (i) reacting an aryl compound selected from an arylalkyl halide having general formula I, aryl alcohol having general formula II or aryl substituted olefins having general formula III, as shown in the accompanying drawings, wherein, R_1 is aryl, substituted aryl, naphthyl or substituted naphthyl groups, R_2 , R_3 , R_4 and R_5 are independently hydrogen, alkyl, aryl, arylalkyl or cycloaliphatic groups with or without substituents and X is ~~[other]~~ a halogen atom selected from chlorine, bromine~~[,]~~ or iodine with a halide promoter, an organic acid, water and a palladium catalyst in an organic solvent selected from ketones or cyclic ethers in carbon monoxide atmosphere under homogeneous conditions, at a temperature ranging between 30 to 130°C, for a period ranging between 0.3 to 4 hrs, at pressures ranging between 50 to 1500 psig,
 - (ii) cooling the reaction mixture to an ambient temperature,
 - (iii) flushing the reaction vessel with an inert gas,
 - (iv) removing the solvent by conventional methods, and separating the catalyst and isolating 2-aryl propionic acid having formula (IV) as shown in the accompanying drawings, wherein, R_1 is aryl, substituted aryl, naphthyl or substituted naphthyl groups, R_2 , R_3 , R_4 and R_5 are independently

20 represented by hydrogen, alkyl, aryl, arylalkyl, cycloaliphatic groups with or
 21 without substituents.

Claim 2 has been amended as follows:

1 2. A process as claimed in claim 1, wherein catalyst is selected from the group of
 2 palladium(O) or palladium(II) compound comprising palladium chloride, palladium
 3 bromide, palladium iodide, ~~[bis(triphenylphosphino) dichloro palladium(II);~~
 4 ~~bis(triphenylphosphino) dibromo palladium(II);]~~ bis(triparatolylphoshino) dichloro
 5 palladium(II), ~~{bis(tricyclohexylphosphino) dichloro palladium(II);}~~
 6 bis(triethylphosphino) dichloro palladium(II), bis(triisopropylphosphino) dichloro
 7 palladium(II), ~~{tetrakis(triphenylphosphino) palladium(O);}~~ dibenzylideneacetato-
 8 palladium(O), cyclooctadiene dichloro palladium(II), bisbenzonitriledi-chloro
 9 palladium(II), acetylacetonato palladium(II) and bisacetonitrile dichloro
 10 palladium(II).

Claim 7 has been amended as follows:

1 7. A process as claimed in claim 1 wherein in step (I) the organic solvent is selected
 2 from the group of ketones comprising methyl ethyl ketone, methyl isobutyl ketone,
 3 diethyl ketone, methyl n-propyl ketone, acetophenone or cyclic ethers ~~{such as~~
 4 ~~tetrahydrofuran, dioxan}~~.

The following new claim has been added:

1 20. A process as claimed in claim 7, wherein the cyclic ethers are tetrahydrofuran and
 2 dioxan.